AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions and listings of claims in the application:

1. (Withdrawn) A sulfur atom-free enzyme protein comprising 18 types of L-amino acid residue: L-alanine; L-aspartic acid; L-glutamic acid; L-phenylalanine; L-glycine; L-histidine; L-isoleucine; L-lysine; L-leucine; L-asparagine; L-proline; L-glutamine; L-arginine; L-serine; L-threonine; L-valine; L-tyrosine; and L-tryptophan.

2. (Withdrawn) The sulfur atom-free enzyme protein according to claim 1 which retains the activity of the original enzyme protein and has oxidation resistance, wherein L-cystein and L-methionine residues in enzyme proteins comprising 20 types of L-amino acid residue: L-alanine; L-aspartic acid; L-glutamic acid; L-phenylalanine; L-glycine; L-histidine; L-isoleucine; L-lysine; L-leucine; L-asparagine; L-proline; L-glutamine; L-arginine; L-serine; L-threonine; L-valine; L-tyrosine; L-tryptophan; L-cystein; and L-methionine, are substituted with 18 types of L-amino acid residue: L-alanine; L-aspartic acid; L-glutamic acid; L-phenylalanine; L-glycine; L-histidine; L-isoleucine; L-lysine; L-leucine; L-asparagine; L-proline; L-glutamine; L-arginine; L-serine; L-threonine; L-valine; L-tyrosine; and L-tryptophan.

3. (Withdrawn) The sulfur atom-free enzyme protein according to claim 2 wherein amino acid substitution is carried out by site-directed mutagenesis using synthetic DNA.

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4. (Withdrawn) The sulfur atom-free enzyme protein according to any one of claims 1 to 3 wherein the enzyme activity is oxidation-reduction activity or hydrolysis activity.

5. (Withdrawn) The sulfur atom-free enzyme protein according to any one of claims 1 to 4, which retains the activity of dihydrofolate reductase and has oxidation resistance.

6. (Withdrawn) The sulfur atom-free enzyme protein according to any one of claims 1 to 4, which retains the activity of xylanase and has oxidation resistance.

7. (Currently amended) A method of producing a sulfur atom-free enzyme protein having activity greater than or equivalent to an original enzyme protein, wherein the sulfur atom-free enzyme protein is prepared by a combined mutation method comprising ~~the following steps~~:

(1) preparing a mutant gene by substituting an initiation codon encoding L-methionine in a DNA sequence encoding an enzyme protein ~~consisting of a total length of m amino acids, and~~ having an amino acid sequence comprising n number of sulfur atom-containing amino acids ~~(sulfur-containing amino acids)~~, wherein a position of a sulfur-containing amino acid on the sequence is Ai (i = 1 to n), ~~by~~ with codons encoding any of L-methionine-L-alanine, L-methionine-L-serine, or L-methionine-L-proline ~~codon~~;[[,]] expressing the ~~prepared~~ mutant gene in a host cell to obtain a mutant enzyme protein;[[,]] measuring enzyme activity of the ~~obtained~~ mutant enzyme protein;[[,]] and

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selecting the mutant enzyme protein with the highest activity, thereby obtaining a ~~substitution~~ mutant enzyme protein having a substitution A1/MA1;

(2) preparing a mutant gene in which ~~codons~~ a codon encoding a sulfur-containing amino acid[[s]] at ~~another sites~~ a position Ai (i = 2 to n) ~~are~~ is substituted with a codon[[s]] encoding ~~another amino acids among the 18 types of amino acid according to claim 1,~~ any of L-alanine, L-aspartic acid, L-glutamic acid, L-phenylalanine, L-glycine, L-histidine, L-isoleucine, L-lysine, L-leucine, L-asparagine, L-proline, L-glutamine, L-arginine, L-serine, L-threonine, L-valine, L-tyrosine, and L-trypotophan, for a maximum of 18 different substitutions at any Ai;[[,]] expressing the ~~prepared~~ mutant gene in a host cell to obtain a mutant enzyme protein; measuring enzyme activity of the ~~obtained~~ mutant enzyme protein;[[,]] and selecting ~~p number of mutant enzyme proteins having enzyme activity, thereby obtaining substitution mutants Ai/Bij (j = 1 to p);~~

~~(3) selecting a maximum of 3 substitution mutants~~ a maximum of three mutant enzyme proteins having the highest activity, thereby obtaining mutant enzyme proteins having substitutions Ai/Bi1, Ai/Bi2, and Ai/Bi3, wherein activity decreases in order[[,]] Ai/Bi1>Ai/Bi2>Ai/Bi3;~~>...>Ai/Bip; and~~

(3) repeating (2) for all Ai; and

(4) ~~selecting substitution mutants having activity in respect of sulfur-containing amino acids at all sites Ai (i = 2 to n) in the same manner as (2) and (3) above, preparing a maximum of 3 x (n-i) mutants being all combinations of these mutants with the mutant~~ producing a sulfur atom-free enzyme protein comprising any combination of the substitutions in (2) and (3) with the

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substitution of A1/MA1 in (1), wherein a substitution occurs at all Ai;[[,]] measuring ~~the~~ enzyme activity ~~thereof~~ of the sulfur atom-free enzyme protein;[[,]] and ~~obtaining~~ selecting a ~~mutant~~ sulfur atom-free enzyme protein having activity greater than or equivalent to that of the original enzyme protein.

8. (Currently Amended) A method of producing a sulfur atom-free enzyme protein having activity greater than or equivalent to an original enzyme protein, wherein the sulfur atom-free enzyme protein is prepared by a stepwise mutation method comprising ~~the following steps~~:

(1) preparing a mutant gene by substituting an initiation codon encoding L-methionine in a DNA sequence encoding an enzyme protein ~~consisting of a total length of m amino acids, and~~ having an amino acid sequence comprising n number of sulfur atom-containing amino acids ~~(sulfur-containing amino acids)~~, wherein a position of a sulfur-containing amino acid on the sequence is Ai (i = 1 to n), ~~by~~ with codons encoding any of L-methionine-L-alanine, L-methionine-L-serine, or L-methionine-L-proline ~~codon,~~; expressing the ~~prepared~~ mutant gene in a host cell to obtain a mutant enzyme protein;[[,]] measuring enzyme activity of the ~~obtained~~ mutant enzyme protein;[[,]] and selecting the mutant enzyme protein with the highest activity, thereby obtaining ~~a substitution~~ an A1/MA1 mutant ~~A1/MA1~~;

(2) preparing a mutant gene in which ~~codons~~ a codon encoding a sulfur-containing amino acid[[s]] at A2 of the A1/MA1 mutant of (1) is substituted with a codon encoding ~~another amino acid~~ any of L-alanine, L-aspartic acid, L-glutamic acid, L-phenylalanine, L-glycine, L-histidine, L-

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isoleucine, L-lysine, L-leucine, L-asparagine, L-proline, L-glutamine, L-arginine, L-serine, L-threonine, L-valine, L-tyrosine, and L-trypotophan, for a maximum of 18 different substitutions at A2; ~~being one of the 18 types of amino acid according to claim 1,~~ expressing the ~~prepared~~ mutant gene in a host cell to obtain a double mutant;[[,]] measuring enzyme activity of the ~~obtained~~ double mutant ~~enzyme protein,~~; and selecting a maximum of 3 ~~triple~~ double mutants with the highest activity;

(3) preparing a mutant gene in which a codon encoding a sulfur-containing amino acid at ~~each~~ A3 of the ~~obtained~~ double mutants is substituted with a codon encoding ~~another amino acid~~ any of L-alanine, L-aspartic acid, L-glutamic acid, L-phenylalanine, L-glycine, L-histidine, L-isoleucine, L-lysine, L-leucine, L-asparagine, L-proline, L-glutamine, L-arginine, L-serine, L-threonine, L-valine, L-tyrosine, and L-trypotophan, for a maximum of 18 different substitutions at A3; ~~being one of the 18 types of amino acid according to claim 1,~~ expressing the ~~prepared~~ mutant gene in a host cell to obtain a triple mutant;[[,]] measuring enzyme activity of the ~~obtained~~ triple mutant ~~enzyme protein,~~; and selecting a maximum of [[3]] three triple mutants with the highest activity; and

(4) repeating the stepwise substitution of codons encoding sulfur containing amino acids at each remaining Ai (i = 4 to n) in the same manner as ~~described above~~ in (2) and (3), wherein positions Ai-An are substituted in any order; ~~preparing a quadruple mutant, ..., multiple number of n mutant, inspecting~~ measuring enzyme activity of ~~last multiple number of n mutant,~~ a sulfur atom-free enzyme protein obtained upon substitution of An; and ~~preparing~~ selecting a

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~~mutant~~ sulfur atom-free enzyme protein having activity greater than or equivalent to that of the original enzyme protein.

9. The process for producing a sulfur atom-free enzyme protein prepared by the stepwise mutation method ~~according to~~ of claim 8 wherein A1-An are substituted in order of position on the amino acid sequence ~~the order of stepwise mutation sites is according to any one of (n! types) permutations and combinations of A1, A2, ..., An~~.

10. (Currently amended) A process for producing a sulfur atom-free enzyme protein using a combination of a combined mutation method and a stepwise mutation method, wherein the method comprises:~~, in an enzyme protein consisting of a total length of m amino acids and comprising n number of sulfur-containing amino acids, in which a site of a sulfur-containing amino acid on the sequence is Ai (i = 1 to n), a process according to claim 7 is adopted at k number of sites and a process according to claim 9 is adopted at remaining n – k number of sites.~~

(1) preparing a mutant gene by substituting an initiation codon encoding L-methionine in a DNA sequence encoding an enzyme protein having an amino acid sequence comprising n number of sulfur atom-containing amino acids, wherein a position of a sulfur-containing amino acid to be substituted is designated as Ai (i = 1 to k, k ≤ n), with codons encoding any of L-methionine-L-alanine, L-methionine-L-serine, or L-methionine-L-proline; expressing the mutant gene in a host cell to obtain a mutant enzyme protein; measuring enzyme activity of the mutant enzyme protein; and selecting the protein with the highest activity, thereby obtaining a mutant enzyme protein having a substitution A1/MA1;

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(2) preparing a mutant gene in which a codon encoding a sulfur-containing amino acid at a position Ai (i = 2 to k) is substituted with a codon encoding any of L-alanine, L-aspartic acid, L-glutamic acid, L-phenylalanine, L-glycine, L-histidine, L-isoleucine, L-lysine, L-leucine, L-asparagine, L-proline, L-glutamine, L-arginine, L-serine, L-threonine, L-valine, L-tyrosine, and L-trypotophan, for a maximum of 18 different substitutions at any Ai; expressing the mutant gene in a host cell to obtain a mutant enzyme protein; measuring enzyme activity of the mutant enzyme protein; and selecting a maximum of three mutant enzyme proteins having the highest activity, thereby obtaining mutant enzyme proteins having substitutions Ai/Bi1, Ai/Bi2, and Ai/Bi3, wherein activity decreases in order Ai/Bi1>Ai/Bi2>Ai/Bi3; and

(3) repeating (2) for all Ai;

(4) producing a mutant enzyme protein comprising any combination of substitutions as in (1), (2), and (3), wherein a substitution occurs at all Ai; measuring enzyme activity of the mutant enzyme protein; and selecting a maximum of three mutant enzyme proteins having the highest activity; and

(5) producing a sulfur atom-free enzyme protein by subjecting the mutant enzyme proteins selected in (4) to stepwise substitution of the remaining n - k number of sulfur-containing amino acids as in claim 8; measuring the enzyme activity of the sulfur atom-free enzyme protein; and selecting a sulfur atom-free enzyme protein having activity greater than or equivalent to that of the original enzyme protein.

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